REMARKS

Applicants respectfully request reconsideration of the application in view of the remarks that follow.

I. Status of the Claims and Amendments

Claim 130 is canceled without prejudice or disclaimer.

Claims 129, 141, 143, and 145 are amended. Claim 129 is amended to recite the subject matter of canceled claim 130 and to recite "a product" rather than "the product." Claim 141 has been amended to replace the phrase "comprises at least 1.5% by weight polyacrylamide, less than 10% by weight polyacrylamide" with the phrase "comprises at least 1.5% by weight but less than 10% by weight polyacrylamide." Claim 143 has been amended to recite that the hydrogel is injected "under" the submucosa of the urethra. Claim 145 has been amended to recite that the hydrogel further comprises cells. Exemplary support for these amendments can be found in the specification as published (U.S. Published Patent Appl. No. 2003/0077244) at paragraphs [0018], [0019], [0041], and [0032] and in original claims 18 and 19. No new matter is being added.

Upon entry of the amendment, claims 129 and 131-147 will be pending and subject to examination on the merits.

II. Miscellaneous Matters

Applicants submit with this a response a copy of the Declaration of Roger R. Dmochowski Under 37 C.F.R. § 1.132, previously filed on 11 June 2008, because the version of this declaration available on PAIR is of poor quality. Thus, the copy is submitted to ensure that the Office has a copy of the declaration that can be easily read.

Also, Applicants would appreciate any assistance the Examiner can provide in updating the Office records to reflect the correct attorney of record. The undersigned filed a power of attorney on 4 June 2008 appointing the registered attorneys and agents associated with customer number 22428. The power of attorney was not accepted, because a certificate as required by 37 C.F.R. § 3.73(b) had not been received. *See* Notice Regarding Power of Attorney dated 9 June 2008. The undersigned submitted a Statement Under 37 C.F.R. § 3.73(b) on 23 December 2008, but the Office records have not been updated to reflect that the undersigned is an attorney of

record. Accordingly, Applicants would appreciate any assistance the Examiner could provide in updating the Office records to reflect that the undersigned is an attorney of record.

III. Claim Rejections – 35 U.S.C. § 112, First Paragraph

Claims 143 and 145 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Office Action, at pages 3 and 4, paragraph 4. According to the Examiner, the recitation in claim 143 that the hydrogel is injected into the submucosa of the urethra is allegedly new matter "since the original specification envisioned injecting the hydrogel 'under the submucosal membrane of the urethra. . . .'" Office Action, at page 3, paragraph 4, lines 5-8. With respect to claim 145, the Examiner also states that paragraph [0032] of the specification "envisions the hydrogel to contain cells and not that the injection step comprises introduction of cells." Office Action at page 4, paragraph 4, lines 4-5.

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended claim 143 to recite that the hydrogel is injected "under the submucosa of the urethra." Claim 145 has been amended to recite that the hydrogel further comprises cells. Thus, the amendments render moot the grounds of rejection under 35 U.S.C. § 112, first paragraph.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of these grounds of rejection.

IV. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 129-147 stand rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. According to the Examiner, (i) there is insufficient antecedent basis for the limitation "the product" in line 3 of claim 129, (ii) claim 141 recites two values of polyacrylamide and it is allegedly unclear how there could be present two different amounts for the same acrylamide compound, (iii) and it is confusing how the step of injecting recited in claim 145 comprises "introduction" of cells. Office Action at page 4, paragraphs 6-8.

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicants have amended claim 129 to replace the phrase "the product" with "a product." Claim 141 has been amended to replace the phrase "comprises at least 1.5% by weight polyacrylamide,

less than 10% by weight polyacrylamide" with the phrase "comprises at least 1.5% by weight but less than 10% by weight polyacryldamide." As discussed above, claim 145 has been amended to recite that the hydrogel further comprises cells. Thus, the amendments render moot the stated grounds for this rejection.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of these grounds of rejection.

V. Claim Rejections – 35 U.S.C. § 103

The claims stand rejected for alleged obviousness over a number of references, in different permutations. Applicants address each of the grounds of rejections in detail below, but the rejections all suffer from a common, fatal flaw. That is, the rejections are premised on factual conclusions that lack evidentiary support and that, in fact, are directly contradicted by the evidence of record. Because the rejections are premised on incorrect factual conclusions, as established by the declaration evidence, they are untenable and should be withdrawn.

A. The Rejection Over Vogel

Claims 129-147 stand rejected over U.S. Patent No. 6,335,028 to Vogel *et al.* According to the Examiner, "Vogel discloses method of treating urinary incontinence by administering, by injection into esophageal wall or via the urethra and into the wall of the bladder sphincter and urethral wall, acrylamide based hydrogel." Office Action at page 5, lines 3-5. The Examiner contends that either the hydrogels of Vogel inherently possess the recited properties or that the person of ordinary skill in the art had the technical ability and motivation to form hydrogel compositions possessing the recited properties for treating incontinence. *See, e.g.*, Office Action at page 5, lines 12-13; page 6, lines 3-5 and 15-18; and at page 7, lines 10-13. Applicants respectfully traverse this ground of rejection.

Vogel fails to render obvious the claimed invention for at least five reasons. First, the recited hydrogel properties, which allow for the successful treatment of urinary incontinence, are not inherent in Vogel's microparticles due to the very different polymers employed by Vogel. Second, Vogel fails to teach or suggest each and every element of the claimed invention in failing to teach or suggest a "hydrogel." Vogel teaches administration of microparticles rather than a "hydrogel." Third, Vogel fails to teach or suggest each and every element of the claimed

invention in failing to teach or suggest "combining acrylamide and methylene bis-acrylamide." Fourth, Vogel fails to teach or suggest each and every element of the claimed invention in failing to teach or suggest a "hydrogel that comprises about 0.5% to 25% by weight of a polymer," even if Vogel's microparticles could be considered a "hydrogel." Vogel's microparticles have a minimum solid content of 27% by weight. Fifth, Vogel fails to teach or suggest each and every element of the claimed invention by failing to teach or suggest the recited molar ratios. Vogel discloses microparticles having a methylolacrylamide:bis-acrylamide molar ratios of about 1.1:1 to about 106:1, which is at least an order of magnitude different than the recited molar ratio. Because of the vast differences between Vogel's microparticles and the recited hydrogel, one of skill in the art would have no reason to modify Vogel to arrive at the claimed invention.

1. The Recited Properties Are Not Inherent To Vogel

The recited "complex viscosity" and "elasticity modulus" are not inherent in Vogel's polymers nor does anything to suggest of one of skill in the art to modify Vogel's polymers to achieve the recited properties. Vogel's microparticles differ from the recited hydrogel in terms of macrostructure, chemical composition, content of polymer, and molar ratios, as discussed below. These differences in the composition of Vogel's polymers would be expected to change the properties of the polymers, including their "complex viscosity" and "elasticity modulus." Accordingly, Vogel's polymers do not *necessarily* have the recited properties, which means that the properties are not "inherent." *See* MPEP § 2112.

The Examiner states that Applicants have "not factually shown that the hydrogel of Vogel cannot have [the recited properties] considering that Vogel specifically uses acrylamide hydrogel to treat urinary incontinence." Office Action at page 8. This contention improperly shifts the Examiner's burden to Applicants. It is the Examiner that must provide a factual basis for believing that some property is inherent in the prior art. *See* MPEP § 2212(IV). Even had the Examiner shouldered this burden, the fact would remain that Applicants have rebutted inherency by showing that the recited characteristics are not necessarily present in Vogel's polymers due to the significant differences in Vogel's microparticles as compared to the recited hydrogel. *See* MPEP § 2112.

2. Vogel Does Not Teach Or Suggest Administering A "Hydrogel"

Vogel does not teach or suggest "injecting into a urethra a hydrogel" for treating urinary incontinence, as claimed. Rather, Vogel generally discusses the use of "microparticles," which are made by forming a gel, then "cut[ting] [it] in small pieces" and grinding the small pieces "to get very small particles." Vogel at Example 6.1. Microparticles, however, are far different from a "hydrogel," as evinced by Christensen *et al.*, AESTHETIC PLASTIC SURGERY 29:34-48 (2005). Christensen demonstrates this art-recognized distinction by noting that there are "[t]hree principally different filler types," including "a homogeneously built polymer gel (silicone gel, polyacrylamide hydrogel)" and "[a] suspension of insoluble polymer or microspheres and a resorbable liquid" Christensen at p. 34, right col. The recited hydrogel is a "a homogeneously built polymer gel," and Vogel's microparticles fall into the latter category, "[a] suspension of insoluble polymer or microspheres." *See* Vogel at Example 6.1 (noting that the gel from which the microparticles were formed "was totally insoluble to water"). Christensen further highlights the distinction between homogeneously built polymer gels and microparticles by highlighting the distinctions between silicone gel and microparticulate silicone. Christensen at p. 35 (compare "Silicone Gel" section to "Polyvinylpyrrolidone-silicone Suspension" section). Accordingly, microparticles, as taught by Vogel, are not considered a "hydrogel," as claimed.

The distinction between a "hydrogel" and Vogel's microparticles is not a mere difference in form – the different types of materials have significantly different properties and biological effects. Christensen generally summarizes the different properties of the types of materials on pages 35-36. Christensen's experimental results bear out the differences in the materials. "The biopsies from the inflammatory nodules differed depending on type of injected filler." Christensen at p. 38, left col. Moreover, Christensen specifically addresses the distinction between homogeneous gels and microparticles. Studies show "a higher production of connective tissue in gels with microsphere or fragments than in homogenous gels." Christensen at p. 44, right col. Also, "homogeneous gels ... elicit a minimal host response," while "combination gels," which contain microspheres, "produce a strong host response." Christensen at p. 44, left col. Christensen, therefore, demonstrates that homogeneous gels have very different biological effects as compared to microparticles.

Because of the significant differences between microparticles and hydrogels, one of skill in the art would not consider Vogel's microparticles to be, or even suggest, a "hydrogel," as

claimed. The claimed method of treating urinary incontinence relies upon administration of a polyacrylamide hydrogel having the recited combination of physical and rheological properties to treat urinary incontinence effectively. Vogel's microparticles are not even a "hydrogel," much less a "hydrogel" having the recited complex viscosity or elasticity modulus, rheological properties that are relevant to hydrogels but wholly inapplicable to Vogel's microparticles. The claimed method of treating urinary incontinence by injecting into the urethra a polyacrylamide hydrogel possessing the recited properties, therefore, would not have been obvious to one of ordinary skill in light in view of Vogel's disclosure regarding microparticles.

3. Vogel Does Not Teach Or Suggest "Combining Acrylamide And Methylene Bis-Acrylamide"

Vogel does not disclose "combining acrylamide and methylene bis-acrylamide," but rather discloses the use of derivatives of acrylamide. Vogel discloses using methylolacrylamide or methylacrylamide derivatives (Examples 6.1 and 6.2) and dimethylacrylamide and a dimethylmethacrylacrylate derivative (Example 6.3). Even the patents purportedly incorporated by reference for teaching methods of polymerization, U.S. Patent No. 5,648,100 and France Patent No. 2,378,808, do not disclose the combination of "acrylamide and methylene bis-acrylamide." Vogel at column 8, lines 37-39. Vogel does mention myriad potential monomers, including acrylamide as a potential monomer and methylene bis-acrylamide as potential difunctional monomer. Vogel at column 7, lines 17-22. Yet Vogel does not suggest the specific combination of the two, as illustrated by the examples. And one of skill in the art would have no reason to select these two from all possible combinations. Indeed, the failure to disclose the combination of the two suggests that Vogel considered the combination unsuitable for its intended purpose. Accordingly, Vogel would not suggest to one of skill in the art "combining acrylamide and methylene bis-acrylamide."

4. Vogel Fails To Teach Or Suggest A "Hydrogel That Comprises About 0.5% To 25% By Weight Of A Polymer"

Vogel does not teach or suggest "a hydrogel that comprises about 0.5% to 25% by weight of a polymer." Even assuming equivalency between Vogel's microparticles and a hydrogel, which is flatly incorrect, Vogel does not suggest the recited weight percent of polymer. Vogel discloses an acrylic copolymer that comprises about 25% to about 98% neutral hydrophilic acrylic monomer by weight, about 2% to about 50% difunctional

monomer by weight, and about 0% to about 50% by weight of one or more monomers having a cationic charge. Vogel at column 7, lines 6-11. Accordingly, Vogel's microspheres have a minimum solid weight content of about 27% weight percent (25% of the acrylic monomer + 2% of the difunctional monomer = 27%, because conversion is near 100%). Because Vogel's minimum solid content is greater than the maximum recited by the claims, Vogel does not teach the recited polymer content. Moreover, the record is devoid of any reason to modify Vogel to arrive at the recited polymer content.

5. Vogel Fails To Teach Or Suggest The Recited Molar Ratio

Vogel discloses the use of implantable microparticles in the treatment of urinary incontinence. The microparticles can comprise an acrylic copolymer that comprises about 25% to about 98% neutral hydrophilic acrylic monomer by weight, about 2% to about 50% difunctional monomer by weight, and about 0% to about 50% by weight of one or more monomers having a cationic charge. Column 7, lines 6-11. In a preferred embodiment, Vogel discloses a copolymer comprising about 25-98% methacrylamide by weight, and about 2-50% N,N-methylene-bis-acrylamide by weight. *Id.*, lines 28-31.

These values can be converted to molar ratios based on the molecular weights of the different monomers, which are provided in Exhibits A-C.[1] Performing the calculations results in acrylamide:bis-acrylamide molar ratios ranging from about 1.1:1[2] to about 106:1.[3] These values fall far outside the recited molar ratios of 150:1 to 1000:1.

Vogel's Example 6.1, the only one describing preparation of an acrylamide hydrogel, confirms that Vogel's copolymers have molar ratios falling far outside the recited range. In

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[1] These calculations assume that the polymerization reaction proceeds to completion or near-completion. Applicants note that the examiner makes the assumption that the polymerization reaction does proceed to completion or near-completion. *See* Office Action, at page 5, lines 12-15. Applicants note that even if this assumption is not accurate, and the weight percentages (wt%) of acrylamide and bis-acrylamide monomers in the copolymers of Vogel do not reflect the weight percentages of the acrylamide and bis-acrylamide starting materials, Example 6.1 of Vogel nevertheless clearly illustrates a polyacrylamide gel falling outside the scope of the present claims, as discussed below.

[2] For 100 g of copolymer, assuming 25 wt% acrylamide ((25 g acrylamide)/(71.1 g/mole) = 0.352 moles acrylamide) and 50 wt% bis-acrylamide ((50 g bis-acrylamide)/(154.2 g/mole) = 0.324 moles bisacrylamide).

[3] For 100 g of copolymer, assuming 98 wt% acrylamide ((98 g acrylamide)/(71.1 g/mole) = 1.38 moles acrylamide) and 2 wt% bis-acrylamide ((2 g bis-acrylamide)/(154.2 g/mole) = 0.0130 moles bis-acrylamide).

Example 6.1, 90 g of methylolacrylamide monomer and 2 g of methacrylamidopropyl-trimethyl-ammonium-chloride hydrochloride monomer are combined with 10 g of N,N'-methylene-bis-acrylamide difunctional monomer. This yields an acrylamide copolymer comprising about 88.2% by weight methylolacrylamide (90 g methylolacrylamide/102 g total acrylamide) and about 9.8% by weight bis-acrylamide (10 g bis-acrylamide /102 g total acrylamide), values within the preferred monomer weight percentage ranges disclosed by Vogel. This corresponds to a 0.89 moles of methylolacrylamide[4] and 0.065 moles N,N'-methylene-bis-acrylamide.[5] Thus, the molar ratio of methylolacrylamide:bis-acrylamide in the copolymer of Example 6.1 is 14:1 – a value over ten-fold less than the minimum acrylamide:bis-acrylamide molar ratio recited by the claims, 150:1.

Because Vogel's polymers have acrylamide:methylene bis-acrylamide molar ratios that are far afield of the presently recited ranges, Vogel fails to teach each element of the claimed invention. Moreover, nothing in Vogel would have suggested employing a polymer having the recited acrylamide:methylene bis-acrylamide molar ratios. Indeed, Vogel's polymers, disclosed as suitable for a certain purpose, are characterized by ratios that differ by at least an order of magnitude from the recited ratios. It is apparent, therefore, that the person of ordinary skill in the art would have had to diverge entirely from Vogel's compositions in order to obtain a polymer having a molar ratio as presently recited; yet, there was no reason in the art for such a divergence, much less a reasonable expectation of success in venturing so far from Vogel's teachings. Accordingly, Vogel's teachings about polymers would not have suggested the recited hydrogel.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

B. Pavlyk and Sknar or Vogel

Claims 129-147 stand rejected over U.S. Patent No. 5,798,096 to Pavlyk in view of RU 2,148,957 to Sknar or Vogel. According to the Examiner, Pavlyk discloses cross-linked polyacrylamide hydrogels meeting the limitations of the acrylamide hydrogels of the claims.

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[4] Calculated using a molecular weight of 101.1 g/mol: (90 g methylolacrylamide) / (101.1 g methylolacrylamide /mole) = 0.89 moles

[5] Calculated using a molecular weight of 154.2 g/mol: (10 g N,N'-methylene-bis-acrylamide) / (154.2 g N,N'-methylene-bis-acrylamide/mole) = 0.065 moles

Office Action at page 8, line 20, to page 9, line 1. The Examiner agrees, however, that Pavlyk "does not [disclose] inject[ing] the hydrogel into the urethra." Office Action at page 10. The Examiner relies on Vogel and Sknar to remedy this deficiency. *Id.* Applicants respectfully traverse these grounds of rejection.

The rejections based on Pavlyk in view of Vogel and Sknar are separately addressed in detail below. But both rejections share a common flaw, in that none of the cited references would suggest one of skill in the art that the recited hydrogel could be used successfully to treat urinary incontinence. Moreover, none of the cited references discloses the recited hydrogel, much less a method for its use in treating urinary incontinence.

1. Pavlyk in view of Vogel

The rejection based on Pavlyk in view of Vogel is flawed for two reasons. First, the person of ordinary skill in the art would have had no reason to substitute Pavlyk's polymer for Vogel's microparticles for the treatment of UI. Second, neither Pavlyk nor Vogel suggests the recited hydrogel.

a. Vogel Does Not Suggest The Use Of Pavlyk's Polymer

The Examiner cited Vogel as treating urinary incontinence, because Pavlyk, as acknowledged by the Examiner, does not disclose the treatment of urinary incontinence. Office Action at page 10, lines 11 and 12. Rather, Pavlyk states that its polymer can be used as a penile implant material. Thus, the Examiner suggests substituting Pavlyk's polymer for Vogel's microparticles.

Fundamental to the rejection is the notion that one of skill in the art would find obvious substituting Pavlyk's polymer for Vogel's microparticles. This notion lacks record support and, in fact, is incorrect. One of skill in the art would not have any reason to substitute Pavlyk's polymer for Vogel's microparticles for the treatment of UI due to the vast differences between the materials. In fact, the references teach away from the claimed combination. *See Ricoh Co., Ltd. v. Quanta Computer Inc.*, 550 F.3d 1325, 1332 (Fed. Cir. 2008) ("[a] reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant").

First, Vogel's polymer is in the form of a suspension of polyacrylamide microparticles, rather than in the form of a continuous, non-particulate hydrogel, as in the claimed method. Microparticles and hydrogels are distinct classes of materials in the art that each have unique rheological and biological properties, as evinced by Christensen.

Second, Vogel fails to teach or suggest "combining acrylamide and methylene bis-acrylamide," but Pavlyk, on the other hand, does disclose this combination. Accordingly, the chemical composition of the materials is different. This difference in basic chemical composition would not lead one of skill in the art to believe that Pavlyk's polymer could be successfully substituted for Vogel's purpose.

Third, Vogel's material has a polymer content of 27-100% by weight, but Pavlyk's hydrogel has a polymer content of 3.5-9% by weight. Again, this difference in polymer content would deter one of skill in the art from using Pavlyk's polymer for Vogel's use.

Fourth, Vogel discloses ranges of monomer that can be used to form its microparticles, and these ranges translate into acrylamide:bis-acrylamide molar ratios ranging from about 1.1:1 to about 106:1, as discussed above. These preferred ranges of monomer would discourage one of skill in the art from departing wildly from the preferred ranges to use a polymer having "a molar ratio of 150:1 to 1000:1," as claimed. If anything, Vogel would have suggested the use of polymers more rigid, highly crosslinked hydrogels, as compared to Pavlyk's polymer, to treat urinary incontinence.

Fifth, because of the differences in chemical composition and structure, Vogel's and Pavlyk's polymers differ in all of the recited rheological properties, complex viscosity and elasticity modulus. Nothing in the references suggests the desirability of the recited properties, so one of skill in the art would have no reason to believe that the use of Pavlyk's hydrogel would be possible, much less successful.

In sum, Pavlyk's polymer differs from Vogel's microparticles in every relevant way – types of material (hydrogel v. microparticles), content of polymer, chemical composition, molar ratio, presence of residual monomer,[6] complex viscosity, and elasticity modulus. One of skill in

[6] Pavlyk's polymer has far more residual monomeric units than permitted by the claims, as shown by the previously submitted declaration of Mr. Lessél.

the art would, therefore, have no reason to substitute Pavlyk's polymer for Vogel's microparticles and would certainly not have any expectation of success in doing so. The suggested substitution is the epitome of hindsight made possible only with the recognition of the claimed invention.

b. Pavlyk Teaches Away From Vogel

Pavlyk discloses microparticles that can be used injected. *See, e.g.*, Vogel at Fig. 1; column 6, lines 44-46. With respect to UI, Vogel states that "[i]mplantation [of microparticles] is generally made using a syringe or other device suitable for the particular tissue of implantation." Vogel at column 4, lines 63-65.

Pavlyk, on the other hand, states the following:

> Concentrations below 3.5% make the hydrogel unstable only to be applied as a base for medicinal ointments or electroconducting immersion media for cardio- or encephalography, while concentrations above 6.0% decrease fluidity of the hydrogel practically to zero and is practicable, in manufacturing relatively firm, form-retaining, precast endoprostheses that require a surgical procedure to have access to the region of placing such an endoprosthesis.

The person of ordinary skill in the art is lead to understood that hydrogels having less than 3.5% polymer are unsuitable and hydrogels having more than 6% requires surgery. Because Vogel's microparticles have a solid weight content of at least 27%, Pavlyk suggests that they cannot be injected as intended. Accordingly, starting from Pavlyk and the teaching that above 6% is not fluid, one is not motivated to increase the solid weight content to that of Vogel. Accordingly Pavlyk teaches away from combining with Vogel.

Furthermore, Pavlyk teaches away from a hydrogel having a polymer content outside 3.5-6%. The claims, however, recite a hydrogel having a polymer content of below 3.5% by weight. Neither Pavlyk nor Vogel suggest that this is possible, and both references, in fact, suggest that this would not be successful. The same is true for compositions above 6 or 9% polymer by weight.

c. *Pavlyk and Vogel Do Not Teach Or Suggest The Recited Hydrogel*

Vogel does not teach or suggest the recited hydrogel, as discussed in Section V(A) above. Generally, Vogel's microparticles differ from the recited "hydrogel" in the following ways:

- Vogel discloses microparticles, which are far different from a "hydrogel;"
- Vogel fails to teach or suggest "combining acrylamide and methylene bis-acrylamide;"
- Vogel fails to teach or suggest a "hydrogel that comprises about 0.5% to 25% by weight of a polymer," even if Vogel's microparticles could be considered a "hydrogel."
- Vogel fails to teach or suggest the recited molar ratios.
- Vogel fails to disclose a hydrogel with the recited rheological properties

Pavlyk also does not teach or suggest the recited polymer as established by Declaration Under 37 C.F.R. § 1.132 by Robert Lessél filed 11 June 2008 "(Lessél Decl."). "Pavlyk makes no mention of removing residual monomer, but rather is intent on identifying decomposition products of the polymer...." Lessél Decl. at ¶ 7. Moreover, Pavlyk's Table 3 shows less than 100% recovery after polymerization, which suggests residual monomer. Lessél Decl. at ¶ 8. The presence of residual monomer was confirmed by replicating Pavlyk's procedures. Lessél Decl. at ¶ 10. These tests show that Pavlyk's polymer would have had a residual monomeric acrylamide content of about 693 pm to 2646 ppm, far greater than the amount of monomer permitted by the claims. Lessél Decl. ¶ 10. Contura's efforts corroborate this finding, because Contura found that Pavlyk's polymers "were characterized by a high residual acrylamide monomer content." Declaration of Dr. Ieva Ankorina-Stark Under 37 C.F.R. § 1.132 ("Ankorina-Stark Decl.") filed 11 June 2008 at ¶ 13. Thus, Pavlyk's polymers must be subjected to a "washing procedure" to reduce the monomer content to the recited level. Ankorina-Stark Decl. at ¶ 14. Pavlyk failed to recognize the presence of residual monomer or its significance. Lessél Decl. at ¶ 11. Accordingly, Pavlyk fails to teach or suggest the recited hydrogel.

The Examiner persists in stating that Pavlyk's polymer "meet[s] the limitations of the acrylamide hydrogels." But this conclusion is incorrect and plainly rebutted by the Lessél and Ankorina-Stark Declarations. The Examiner has not "explain[ed] why this evidence is insufficient," as required. MPEP § 716.01(B); *In Re Sullivan*, 498 F.3d 1345, 1349 (Fed. Cir. 2007) ("[t]he claimed composition cannot be held to have been obvious if competent evidence rebuts the prima facie case of obviousness"). Accordingly, there is insufficient basis to disregard the reasoned opinions and facts established by the declarations.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

2. Pavlyk in view of Sknar

Pavlyk in view of Sknar does not render obvious the claimed invention for two reasons. First, even if combined, Pavlyk and Sknar do not teach or suggest the recited hydrogel. Second, Sknar's injection of polyacrylamide hydrogels into the *ureter* to treat vesicoureteral reflux ("VUR") does not teach or suggest the treatment of urinary incontinence by "injecting into a *urethra* a hydrogel," as claimed.

a. Pavlyk and Sknar Do Not Teach Or Suggest The Recited Hydrogel

Neither Pavlyk nor Sknar suggests the recited hydrogel. Pavlyk's polymer contains far more monomer than permitted by the claims, as discussed above. Sknar fails to provide any details of its polymer, so it is mere speculation that it could somehow meet the requirements of the recited hydrogel. Even if combined, therefore, the references do not fairly teach or suggest the recited polymer.

b. One Of Skill In The Art Would Not Generalize From Use Of Bulking Agents For VUR To Use Of Bulking Agent For Urinary Incontinence

Neither Pavlyk nor Sknar suggests treating urinary incontinence by "injecting into a urethra a hydrogel," as claimed. Sknar discloses injection of polyacrylamide hydrogels into the ureter to treat vesicoureteral reflux ("VUR"), and Pavlyk concerns itself with, among other things, a penile implant material. Nonetheless, the Examiner contends that one of ordinary skill in the art would have generalized a method of treating one condition, VUR, to another, urinary incontinence, on the basis that both involve impeding the flow of urine.

This conclusion is untenable in view of the multiple expert declarations of record, showing that a person of ordinary skill in incontinence treatment would *not* have generalized from the treatment of VUR to treatment of urinary incontinence.

Two experts with impeccable credentials, Drs. Diamond and Dmochowski, submitted declarations explaining that the person of ordinary skill in the art would not have generalized

from the usage of a bulking agent to treat VUR to usage of the agent to treat urinary incontinence. *See* Declaration of David A. Diamond Under 37 C.F.R. § 1.132 ("Diamond Decl.") filed 11 June 2008 and Declaration of Roger R. Dmochowski Under 37 C.F.R. § 1.132 ("Dmochowski Decl.") filed 11 June 2008. Specifically, Dr. Diamond explains that VUR and total urinary incontinence have "very different pathology[ies]," and due to these different pathologies, one of skill in the art "would not have presumed or reasonably expected that a given demonstration of using a bulking agent to correct VUR [...] would be predictive of success in treating pediatric urinary incontinence with that bulking agent." Diamond Decl. at ¶¶ 7-8. Dr. Dmochowski corroborates this opinion by explaining the anatomical differences underpinning the differences between VUR and urinary incontinence. Generally, treatment of VUR requires addressing "a single physical dysfunction, failure of muscular contraction of the UVJ," but treatment of urinary incontinence is far more complex and involves, *inter alia*, both neural and muscular components. Dmochowski Decl. at ¶ 8-11. Because of the significantly different mechanisms implicated by urinary incontinence as compared to VUR, Dr. Dmochowski reasons that one of skill in the art "would not have generalized from (i) documents usage of a bulking agent for treating VUR to (ii) a suggestion of using such a bulking agent to treat UI." Dmochowski Decl. at ¶ 13. Both Drs. Diamond and Dmochowski agree, therefore, that treatment of VUR using a bulking agent does not suggest treating urinary incontinence using the same bulking agent to one of skill in the art.

The Examiner disregards this declaration evidence and reaches the opposite conclusion. Yet she has not sufficiently "explain[ed] why this evidence is insufficient," as required, for instance, by MPEP § 716.01(B). Accordingly, there is insufficient basis to disregard the reasoned opinions and facts established by the declarations.

The Examiner discounts the Diamond Declaration, because "generic claims 91, 111 and 115-117 and the claim dependent therefrom are not directed to treating pediatric urinary incontinence."[7] This argument both misapprehends the Diamond Declaration and fails to give it the proper weight. Dr. Diamond's comments touch on pediatric urinary incontinence simply because Sknar, a reference addressed by Dr. Diamond, is directed to treatment of VUR in children. Dr. Diamond's opinions, however, also apply to urinary incontinence in adults, as

[7] Claims 91, 111, and 115-117 are not pending. Applicants assume the Examiner intends to refer to the pending claims.

explained in the Dmochowski Declaration. Moreover, the Examiner has provided no explanation as to how adult urinary incontinence differs from pediatric urinary incontinence such as to undermine Dr. Diamond's opinions. Accordingly, the Examiner has failed to provide an adequate explanation for disregarding the Diamond Declaration.

The Examiner also argues that "the suggestion by the RU, the Sknar reference, and acceptance by the declaration that, bulking agents have been used to treat VUR and other types of urinary incontinence in children provides a basis for the ordinary skilled artisan to *reasonable* [sic] expect that bulking agents injected into the tube connecting the urinary bladder to the outside would successfully bulk the tube and increase resistance to the flow of urine from the bladder to the outside." Office Action at page 12 (emphasis supplied). This conclusion does not explain how Dr. Diamond's opinions are flawed but merely expresses the opposite opinion. Indeed, Dr. Diamond's opinion eviscerates the very crux of this conclusion by establishing that one of skill in the art would *not* reasonably expect to generalize from treating VUR to urinary incontinence using a bulking agent.

With respect to the Dmochowski Declaration, the Examiner contends that "the declaration appears to ignore the fact that the rejection of the claims is made over a combination of references and not just over the Sknar reference" and that "Sknar is relied upon to show that polyacrylamide hydrogel impedes the flow of urine, the Sknar reference does not categorically say that the polyacrylamide hydrogel would only impede the flow of [u]rine from the ureter back to the kidneys." Office Action at page 12. Dr. Dmochowski clearly recognizes that the rejection is based on multiple references, however, but he opines that the person of ordinary skill in the art "would not have generalized from (i) documents usage of a bulking agent for treating VUR to (ii) a suggestion of using such a bulking agent to treat UI." Dmochowski Decl. at ¶ 13. The fact that Sknar reference may impede urine does nothing to undermine the conclusion that one of skill in the art simply "would not have generalized from [...] usage of a bulking agent for treating VUR to [...] using such a bulking agent to treat UI." Moreover, Sknar's silence on this point certainly does not weigh against the knowledge in the art that bulking agents would not be successful in treating urinary incontinence due to the complex underlying pathology. Again, the Examiner does not explain why the opinions of Dr. Dmochowski are incorrect, but rather improperly seeks to undermine those opinions by simply reaching an opposite conclusion.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

C. Secondary Considerations Undermine Any Conclusion Of Obviousness

In performing its obviousness analysis, the Office must evaluate the record as a whole including any objective evidence of non-obviousness, including unexpected results and the failure of others. Here, the record contains objective evidence of non-obviousness sufficient to vitiate any conclusion of obviousness.

First, the declaration evidence demonstrates that Applicants succeeded where others have repeatedly failed. Prior to Applicants' invention, polyacrylamide was considered unsafe or ineffective as a bulking agent. Ankorina-Stark Decl. at ¶ 8. Moreover, the use of bulking agents was believed to be ineffective for treatment of urinary incontinence. Diamond Decl. at ¶ 6; Dmochowski Decl. at ¶ 12. It was Applicants' initiative, pressing past this conventional wisdom, that led to the development of a polyacrylamide polymer this is suitable and, in fact, highly effective for the treatment of urinary incontinence. Ankorina-Stark Decl. at ¶¶ 12-16. The record thus demonstrates that Applicants overcame biases in the art to succeed where others had failed.

Second, the claimed invention results in unexpected results. As noted above, the use of bulking agents was believed to be ineffective for treatment of urinary incontinence. Diamond Decl. at ¶ 6; Dmochowski Decl. at ¶ 12. Applicants discovered, however, that the recited combination of properties allows for the treatment of urinary incontinence. Accordingly, the claimed invention is characterized by unexpected results.

CONCLUSION

Based on the foregoing, Applicants respectfully request that the Examiner reconsider all rejections and that they be withdrawn. Applicants believe that the application is in condition for allowance, and they solicit an early indication to this effect. Examiner Fubara is invited to contact the undersigned directly, should she feel that any issue warrants further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 C.F.R. §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

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